Is timing of haemorrhage by spectrophotometry similar for haemorrhages in the subdural and subarachnoid space?

We investigated whether quantifying the spectral peaks for oxyhaemoglobin, methaemoglobin, and bilirubin (and their ratios) and comparing them to established standards for timing subarachnoid haemorrhage, might permit timing of the subdural haemorrhage.

When red cells enter the subarachnoid space, they are visible for a few days to several weeks.[1] Lysis of red cells results in oxyhaemoglobin release predominantly between 2 and 12 hours but continues up to 48 hours. A microsomal enzyme haeme oxygenase, released from macrophages (and the arachnoid membrane) converts oxyhaemoglobin to bilirubin. Bilirubin usually appears after 3–4 days but may exceptionally occur as early as 9–10 hours. The ''bilirubin transforming capacity'' is a rate limiting reaction, and when the concentration of oxyhaemoglobin rises rapidly, additional amounts are oxidised non-enzymatically to methaemoglobin.[2]

Thirty spectrograms performed on centrifuged, undiluted samples of subdural aspirates from 14 infants (mean age 4.6 months) admitted with subdural haematoma/effusion of suspected non-accidental origin, were reviewed retrospectively and peaks of oxyhaemoglobin (absorption peak at 413–415 nm), bilirubin (peak at 450–460 nm), and methaemoglobin (absorption peak at 405 nm) identified.

The haemoglobin (Hb) and bilirubin (Bil) spectral amplitudes were converted to micromoles per litre using a nomogram[3] and the Haemoglobin Index [HBI = Hb (μmol/l)/Bil (μmol/l)] and Haemoglobin Coefficient (HC = arc sine$\sqrt{\{[Hb]/[Hb + Bil + 1]\}}$ + arc sine $\sqrt{\{[Hb + 1]/[Hb + Bil + 1]\}}$) calculated on the 30 spectrograms.[4]

Absorbance indices (HBI and HC) of oxyhaemoglobin and bilirubin in subdural specimens did not correspond with those reported for subarachnoid haemorrhage and were unrelated to the time from admission. Pigment concentrations were higher than those reported from patients with subarachnoid haemorrhage, confirming similar observations of Wahlgren and Lindquist who suggested that this was due to ''packing'' of the erythrocytes and their subsequent lysis.[5] Unlike a subarachnoid haemorrhage which disperses within the cerebrospinal fluid spaces and will dilute and disappear fast, the subdural haemorrhage is in a more encapsulated space without a natural circulation.

We concluded that while spectrophotometry of the subdural fluid can identify fresh blood, oxyhaemoglobin, bilirubin, or methaemoglobin in the aspirate, and the presence of bilirubin indicates that bleeding has occurred between 24 hours and 3 days prior to admission, it is not possible to time the original haemorrhage by using spectral peak data from existing models of subarachnoid haemorrhage.

K Kamath Tallur, N R Belton, R Stephen, R A Minns
University of Edinburgh, UK

Correspondence to: Dr R A Minns, Child Life and Health, University of Edinburgh, 20 Sylvan Place, Edinburgh EH9 1UW, UK; Robert.Minns@ed.ac.uk

doi: 10.1136/adc.2003.036061

Competing interests: none declared

References

1 **Tourtelotte W**, Metz LN, Bryan ER, DeJong RN. Spontaneous subarachnoid haemorrhage. *Neurology* 1964;**14**:302–6.
2 **Wahlgren NG**, Lindquist C. Haem derivatives in the cerebrospinal fluid after intracranial haemorrhage. *Eur Neurol* 1987;**26**:216–21.
3 **Kronholm V**, Lintrup J. Spectrophotomeric investigations of the cerebrospinal fluid in the near-ultraviolet region. A possible aid in diseases of the central nervous system. *Acta Psychiatr Neurol Scand* 1960;**35**:314–29.
4 **Marlet JM**, Barreto Fonseca J de P. Experimental determination of time of intracranial haemorrhage by spectrophotometric analysis of cerebrospinal fluid. *Journal Forensic Sci* 1982;**27**:880–8.
5 **Wahlgren NG**, Lindquist C. Haem derivatives in subdural haematomas. *Acta Neurochir (Wien)* 1988;**95**:109–13.

Melatonin and epilepsy

There have been conflicting reports of the effects on seizure control of prescribing melatonin for people with epilepsy.[1–4] We undertook a retrospective before-and-after observational study of 13 young people prescribed melatonin for sleep disturbances at the David Lewis Centre, a residential school for children and young adults with severe epilepsy and learning difficulties situated in Cheshire, UK, with particular focus on any changes in seizure frequency.

At the David Lewis Centre each patient has a comprehensive record of their daily seizure profiles (seizure numbers and seizure types over 24 hours) carefully documented by care workers. Daily seizure rates were tabulated for each young person at 3 months, 1 month, 1 week, and 24 hours before and after the start of melatonin administration. Data were analysed using the Wilcoxon signed ranks test.

Eleven children (aged 6–18 years, mean age 14.1) and two adults were included. All had severe learning disabilities and behavioural problems, 12 had autistic spectrum disorders, and 11 suffered from severe epilepsy. All of the young people had severe sleep disturbance.

The dose of melatonin ranged from 2–6 mg nocte with a mean dose of 4.8 mg (SD 1.54) (0.1 mg/kg/day, SD 0.05). Eleven of the 13 young people slept better with melatonin. Two discontinued melatonin due to lack of efficacy. For the remainder the mean length of time on melatonin was 2.6 years. One person showed worsening behaviour following melatonin initiation, but no other side effects were observed. Of those with epilepsy three had an increase in seizure rate, seven had a decreased seizure rate, and one patient had no observable difference. The Wilcoxon signed ranks test was applied to the data using a significance level of 0.05. The p value was insignificant (>0.05) for all four time parameters, indicating that in this study melatonin had no effect on seizure frequency.

Our experience has been that melatonin can be helpful for sleep disturbance in young people with significant neurological impairment without a demonstrable influence on seizure control.

C Jones
Manchester University, UK

M Huyton
David Lewis Centre, Cheshire, UK

D Hindley
Halliwell Children's Centre, Bolton, UK

Correspondence to: Dr D Hindley, Consultant Paediatrician, Bolton PCT, Halliwell Children's Centre, 1 Aylesford Walk, Bolton BL1 3SQ, UK; dthindley@doctors.org.uk

doi: 10.1136/adc.2005.077172

Competing interests: none

References

1 **Sheldon SH**. Pro-convulsant effects of melatonin in neurologically disabled children. *Lancet* 1998;**351**:1254.
2 **Jan JE**, Hamilton D, Seward N, *et al*. Clinical trials of controlled-release melatonin in children with sleep-wake cycle disorders. *J Pineal Res* 2000;**29**:34–9.
3 **Peled N**, Shorer Z, Peled E, *et al*. Melatonin effect on seizures in children with severe neurologic deficit disorders. *Epilepsia* 2001;**42**:1208–12.
4 **Fauteck J**, Schmidt H, Lerchl A, *et al*. Melatonin in epilepsy: first results of replacement therapy and first clinical results. *Biol Signals Recept* 1999;**8**:105–10.

Nutritional rickets is increasingly diagnosed in children of ethnic origin

We noted with interest the article published by Ladhani and colleagues[1] highlighting the problem of vitamin D deficiency. We agree that this remains a problem, especially in ''at risk'' ethnic minority groups.

In Oldham, which has a population of 49 992 children, 20.8% are Asians (Census 2001). Between December 2002 and March 2004, we identified nine cases of hypocalcaemia/rickets secondary to vitamin D deficiency. We excluded those with vitamin D deficiency secondary to other conditions of non-nutritional aetiologies. All of the nine children had biochemical changes of raised alkaline phosphatase and levels of 25-OHD below 10 ng/ml; three had radiological evidence of rickets. Eight were of Asian origin and five were male.

Presentation of these children was divided into those with hypocalcaemic symptoms and those with clinical rickets. Six of them presented with hypocalcaemic symptoms and their ages ranged from 6 days to 13 years of age. These included two neonates who presented with focal seizures; two toddlers under 2 years who presented with generalised seizures; and two 13 year olds who presented with cramps/carpopedal spasms. Three of the nine presented with signs of rickets and were aged 15–19 months.

The two neonates involved were born at term with their birth weights on the 25th centiles. Calcium levels were 1.39 and 1.54 mmol/l respectively. Both were on formula feeds, and tests on maternal blood revealed levels of parathyroid hormone and calcium suggestive of vitamin D deficiency. Four toddlers were still breast fed, all of whom were confirmed from dietary history to have limited solid intake. Of the two teenagers, one had a diet low in calcium and the other had background problems of abdominal pain.

All the children were treated with vitamin D, and three children also received oral calcium supplements. All responded to treatment with normalisation of biochemical bone profiles and vitamin D/parathyroid hormone levels.

There is no information on the prevalence of rickets in the UK; however, there are reports to say that this is growing.[2] Our

experience and reports across the UK show that the ethnic minority population still remains at risk of vitamin D deficiency. Efforts to promote vitamin D supplementation as recommended by the Department of Health[3] need to be implemented and targeted at the risk group.

E Odeka, J Tan
Royal Oldham Hospital, Rochdale Road, Oldham OL1 2JH, UK; egware@aol.com

References

1 **Ladhani S**, Srinivasan L, Buchanan C, *et al*. Presentation of vitamin D deficiency. *Arch Dis Child* 2004;**89**:781–4.
2 **Mughal MZ**. Resurgence of vitamin D deficiency rickets in the UK. *Osteoporosis Review* 2005;**13**(1):10–13.
3 **Department of Health, Nutrition and Bone Health: with particular reference to calcium and vitamin D**. Report of the Subgroup on Bone Health, Working Group of the nutritional Status of the Population of the Committee on Medical Aspects of the Food Nutrition Policy. *Rep Health Soc Subj (Lond)* 1998;**49**:iii–vii,1–24.

A vaccine scare in 19th century Northampton

The controversy regarding immunisation is longstanding. Records from 1806 concerning a vaccine scare in Northampton give a flavour of events, which strike a contemporary chord.

The revelation of Edward Jenner's 1798 seminal work meant smallpox mortality fell from 31% in unvaccinated children compared to 1.2% in vaccinated.[1 2]

Northampton General Infirmary made cowpox vaccination a high priority and was proactive in its approach, with free cowpox inoculation being undertaken on the hospital premises from 1804 onwards.[3]

On 10 January 1806 the Board of Governors dealt with a growing vaccine scare concerning alleged vaccine failure and one in particular, leading to the death of a child, Peter Bell.

> ''Gentlemen, the public mind having been lately much agitated by reports of the insecurity of the vaccine inoculations, we have endeavoured to investigate those instances of failures we have heard of and have invariably found such reports to be arrived at either by error or misrepresentation.''[3]

However, to defuse the situation an affidavit signed by the parents of Peter Bell denying these rumours was published in the *Northampton Mercury*:[3]

> **Article from the *Northampton Mercury*, 10 January 1806**
> ''Whereas a false and groundless report has been spread about this town and neighbourhood that our son Peter Bell died on the 6th instant of smallpox after having been inoculated for the cowpox by Dr Kerr and the Infirmary now we do hereby declare that neither the above named child nor our child Ann Bell ever had the smallpox or the symptom or appearance of smallpox whatever. Both our said children were inoculated for the cowpox by Mr. Mills and both of them came safely through the disease. The eldest of them has been ever since in perfect health and Peter the youngest having been always a weakly child had better health after the cowpox than ever he had enjoyed before until he was seized with a violent complaint in his bowels of which he died on 20th December last.'' (Signed by William Bell, guard to the Defiance coach; Sarah Bell, his wife[3])

The following week on 17 January the Board of Governors reported.

> ''The Governors…having adopted the resolution of permitting the poor to be inoculated for the cowpox as outpatients…do hereby certify that we know of no incidence of any person having had the smallpox who had been previously inoculated for the cowpox.''[3]

A register was however established with the hope: ''By these means the practice of vaccination and its merits as a complete security against the smallpox will be gradually be brought to the test of unprejudiced experience''.[3]

One could regard this as common sense, which today would be described as ''clinical governance''.

Doctors beleaguered in the present time through similar ''misrepresentations'' regarding immunisations should take heart that this is not a new problem, but perhaps managers could learn from the more robust attitude taken by our medical forebears when dealing with the media in these matters.

A N Williams
Child Development Centre, Northampton General Hospital, Northampton NN1 5BD, UK; anw@doctors.org.uk

doi: 10.1136/adc.2005.081034

Competing interests: none declared

References

1 **Jenner E**. *An inquiry into the causes and effects of the variolae vaccine*. London: Sampson Low, 1798.
2 **Sheldon W**. *Diseases of infancy and childhood*. London: JA Churchill Ltd, 1948:715.
3 **Waddy FF**. *A history of Northampton General Hospital 1743–1948*. Northampton: The Guildhall Press, 1974:57–8.

More evidence is needed in the antibiotic treatment of *Pseudomonas aeruginosa* colonisation

In presenting various therapeutic approaches for the management of cystic fibrosis (CF), Smyth primarily considers evidence obtained from The Cochrane Library as either systematic reviews of randomised controlled trials (RCTs) or RCTs.[1] The antibiotic treatment of *Pseudomonas aeruginosa* (PA) when first isolated, is still an open question. When discussing this aspect, Smyth considers only the RCT by Valerius and colleagues.[2]

In our critical review of published clinical studies evaluating the early antibiotic treatment in asymptomatic PA colonised CF patients,[3] we identified three relevant RCTs (two versus placebo).[2 4 5] Our study also included eight cohort studies, two of which were with historical controls. Overall, 309 patients (range 7–91) were recruited. There was a high variability between the individual studies for age, outcome measures, duration of follow up, and treatment (three studies: two RCTs; 1 cohort used only aerosol tobramycin, 1 colistin, 4 aerosol colistin plus ciprofloxacin, 1 intravenous treatment, and 2 miscellaneous therapy).

An overall critical evaluation indicated that early antibiotic treatment can reduce the rate of positive cultures and of anti-PA antibody titres. Long term benefit is expected but not yet proven. Moreover, we recently conducted an observational study which found that nearly all CF centres in Italy treat asymptomatic PA colonised patients in order to prevent or postpone chronic pulmonary infection (unpublished data). However, the adopted prescribing practice varies largely even within the same centre, highlighting the existing lack of formal consensus on this subject.

Several therapeutic options (aerosol therapy alone or oral therapy associated with aerosol inhalation) are available for the early treatment of PA colonisation, but no direct comparison has so far been made. Prospective multicentre randomised studies with relevant outcomes measures[6] are needed to investigate which of the different proposed antibiotic schemes has the best benefit/risk ratio and the best patient compliance.

F Marchetti, J Bua
Department of Pediatrics, Institute of Child Health, Burlo Garofolo, Trieste, Italy; fedemarche@tin.it

References

1 **Smyth RL**. Diagnosis and management of cystic fibrosis. *Arch Dis Child Ed Pract* 2005;**90**:ep1–ep6.
2 **Valerius N**, Koch C, Hoiby N. Prevention of chronic Pseudomonas aeruginosa colonisation in cystic fibrosis by early treatment. *Lancet* 1991;**338**:725–6.
3 **Marchetti F**, Giglio L, Candusso M, *et al*. Early antibiotic treatment of pseudomonas aeruginosa colonisation in cystic fibrosis: a critical review of the literature. *Eur J Clin Pharmacol* 2004;**60**:67–74.
4 **Wiesemann HG**, Steinkamp G, Ratjen F, *et al*. Placebo-controlled, double-blind, randomized study of aerosolized tobramycin for early treatment of Pseudomonas aeruginosa colonization in cystic fibrosis. *Pediatr Pulmonol* 1998;**25**:88–92.
5 **Gibson RL**, Emerson J, McNamara S, *et al*. Significant microbiological effect of inhaled tobramycin in young children with cystic fibrosis. *Am J Respir Crit Care Med* 2003;**167**:841–9.
6 **Ramsey BW**, Boat TF. Outcome measures for clinical trials in cystic fibrosis. *J Pediatr* 1994;**124**:177–92.

Community needlestick injuries may still be dangerous

We read with interest the report by Makwana and Riordan on community needlestick injuries in children.[1] We do not believe, however, that the authors have presented sufficient data to support their conclusion that routine follow up after community needlestick injury is unnecessary.

In their study only 25 children had complete serological follow up. Their literature review cites three additional papers in which children were followed up after needlestick injury. Adding all of these children gives a total of 138 children who had